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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/358,141    07/20/99    SAMPSON

J    10990393-1

EXAMINER
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SCHMIDT, M

ART UNIT	PAPER NUMBER
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1635

DATE MAILED:

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022878  
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HM12/0523

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

# Office Action Summary

Application No.

09/358,141

Applicant(s)

SAMPSON, JEFFREY R.

Examiner

Mary Schmidt

Art Unit

4636 1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 03/02/01.
- 2a) ☐ This action is **FINAL**.
- 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 11-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

- 15) ☒ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 18) ☐ Interview Summary (PTO-413) Paper No(s) \_\_\_\_\_
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

### DETAILED ACTION

1. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Further, the Brief Description of the Drawings needs to reference the sequences in the Figures by SEQ ID NO.

2. Claims 11-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 11.

Applicant's election with traverse of Group IA in Paper No. 11 is acknowledged. The traversal is on the ground(s) that Applicant be allowed a "reasonable number of species." Specifically, that "the smallest intricacies of molecular mechanisms by which the enumerated species accomplish the polymerization of the precursors is NOT part of the claimed subject matter... nor are the molecular-level intricacies of mechanism of the enumerated species of any

practical consequence to the subject matter claimed... more is needed to support a restriction requirement." This is not found persuasive because the claims are drawn to methods of synthesizing the unstructured nucleic acids by the action of the claimed species of enzymes. It is well-known in the art that different polymerase enzymes have different structural characteristics which lend to different functions of the polymerases. It is not expected that every polymerase in the art will polymerize any modified nucleic acid for synthesis of any unstructured nucleic acid as broadly claimed. Note U.S. Patent 6,184,364, which teaches in col. 8, lines 31-41, that "both 2' amino and 2'-fluoro nucleoside 5'triphosphates are substrates for T7 RNA polymerase, albeit with somewhat decreased incorporation efficiency... 2'-substituted nucleotides such as 2'-O-methyl, 2'-O-alkyl, or 2'-deoxy nucleoside triphosphates are not recognized as substrates by T7 RNA polymerase."

The requirement is still deemed proper and is therefore made FINAL.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are drawn to methods of making "unstructured" nucleic acids. The term "unstructured" is unclear since all nucleic acids must have some structure. It appears that the invention is drawn to methods of reducing secondary structure in nucleic acids, such as reducing hairpin loops, but such compositions retain a structure and therefore can not be considered "unstructured." In view of this language the metes and bounds of the claimed invention are unclear.

The claims further specify providing nucleotide precursors "sufficient" to synthesize an unstructured nucleic acid... which nucleic acid precursors include "pairs of complementary precursors that are unable to hybridize with one another." It is not clear from the claim language whether both precursors are modified, or whether just one precursor is modified. The language "sufficient to synthesize" suggests that the precursors are doing the work of synthesizing the unstructured nucleic acid instead of the enzyme in the step below. The steps of the claims are therefore not clearly written.

Further, in claim 1, "nucleotide precursors" is not defined such that one skilled in the art would understand the metes and bounds of the structures of said precursors. "Nucleic acid precursors" in claim 1 lacks antecedent basis.

Claims 2-8 refer to "nucleotides" and not "nucleotide precursors" thus there is a lack of antecedent basis for "nucleotides". Claims 3-8 specify particular precursors (2-aminodeoxy ATP, 2-thiodeoxy TTP, deoxy ITP, deoxy pyrrolopyrimidine TP, 2- thio deoxy CTP, deoxy GTP, deoxy CTP, deoxy ATP and deoxy TTP) but also specify "or combinations thereof." Since the

purpose of the invention is to create nucleic acids which have sequences that do not bind to each other, can any of the above precursors bind to any of the other specified precursors? It is not clear whether "combinations thereof" encompasses every possible combination of the groups. Thus the metes and bounds of the claims are not clear.

At the end of claim 1, the last step does not clearly relate back to the preamble of the claim. Specifically, the claim specifies "so that said first complementary sequence element and said second complementary sequence element of the unstructured nucleic acid do not interact with one another" and does not specifically claim synthesis of the 'unstructured' nucleic acid.

In claim 9, the preamble of the claim is not written correctly.

Claim 10 does not further limit claim 1 since how the UNA is used does not further limit how it is made.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the

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art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to methods of synthesizing an unstructured nucleic acid. In view of the 35 U.S.C. 112, second paragraph, rejection above, it is assumed that all nucleic acids have some structure, and that the invention is drawn to methods of reducing secondary structure in a target nucleic acid. More specifically it is assumed that the 'unstructured' nucleic acid is a modified RNA since the elected species of enzyme was an RNA polymerase.

All of the claimed precursors (2-aminodeoxy ATP, 2-thiodeoxy TTP, deoxy ITP, deoxy pyrrolopyrimidine TP, 2- thio deoxy CTP, deoxy GTP, deoxy CTP, deoxy ATP and deoxy TTP) are known in the art but are typically made by chemical synthesis and not by enzymatic reaction of an RNA polymerase. Further, the dCTP, dGTP, dATP and DTTP are the natural precursors for making a DNA nucleic acid, not an RNA nucleic acid, and dITP is often used in sequence reactions of DNA.

The claims are not enabled for use of an RNA polymerase for synthesizing any 'unstructured' nucleic acid as claimed in view of the lack of clarity of the claimed invention (it is not clear which precursors to use and in what combination) and the unpredictability in the art for incorporation of any modified precursor via an RNA polymerase as broadly claimed. The specification as filed teaches by way of example use of a DNA Polymerase (Bst) for incorporation of D and S modified nucleotides. As cited above, Pieken et al. teach that "2'-substituted nucleotides such as 2'-O-methyl, 2'-O-alkyl, or 2'-deoxy nucleoside triphosphates are not

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recognized as substrates by T7 RNA polymerase." (U.S. Patent 6,184,364) Since an RNA polymerase will not incorporate deoxy-- precursors, but rather ribose-- precursors, one skilled in the art would necessarily practice an undue amount of experimentation to find modified precursors that would function to make an 'unstructured' nucleic acid as claimed. Specifically, there is a lack of guidance in both the specification and the art for synthesis of such 'unstructured' nucleic acids, or incorporation of the disclosed precursors via any RNA polymerase.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *John LeGuyader*, may be reached at (703) 308-0447.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group Analyst, *Katrina Turner*, whose telephone number is (703) 305-3413.

M. M. Schmidt  
May 21, 2001

  
ROBERT A. SCHWARTZMAN  
PRIMARY EXAMINER